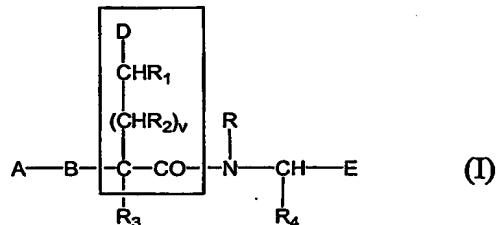


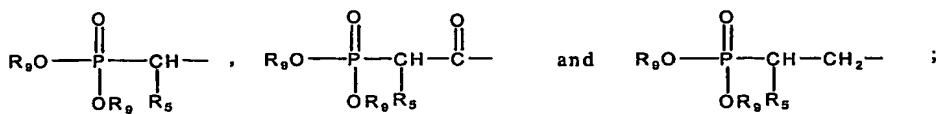
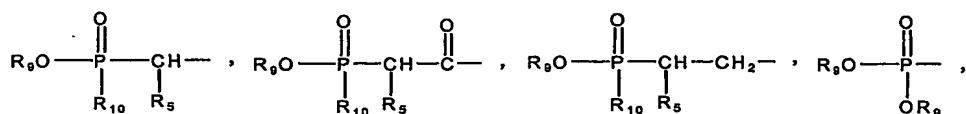
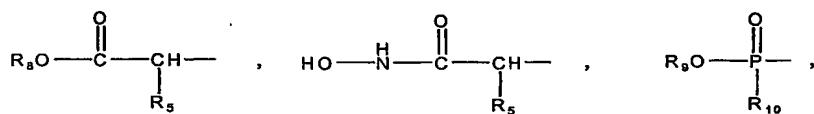
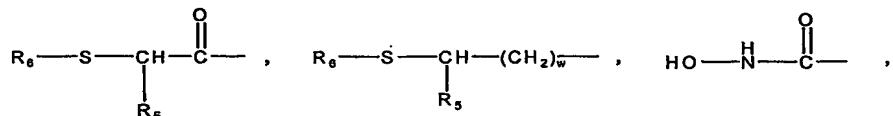
CLAIMS:

1. A compound of Formula (I), or a pharmaceutically acceptable salt thereof:



5 wherein:

A is a zinc ligand or zinc ligand bearing moiety selected from the group consisting of:



B is $\begin{array}{c} R_{11} \\ | \\ -N- \end{array}$, $-\text{CH}_2-$ or absent;

R is hydrogen or lower alkyl ;
R₁ is hydrogen or lower alkyl ;
R₂ is hydrogen, or lower alkyl;
R₁, when v=1, may be connected to the carbon bearing

5 R₂ to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclopropane ring;
R₂, when v=1, may be connected to the carbon bearing
R₁ to form an alkylene bridge of 1 carbon atom representing with the carbon atom to which it is attached a cyclopropane ring;

10 R₃ is hydrogen or lower alkyl;
R₁, when v=1, may be connected to the carbon bearing
R₃ to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring;
R₃, when v=1, may be connected to the carbon bearing

15 R₁ to form an alkylene bridge of 1 carbon atom, representing with the carbon atom to which it is attached a cyclobutane ring;
R₁ and R₃, when v=1, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring;

20 R₁ and R₃, when v=0, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclopentane ring;
R₁ and R₃, when v=0, may be connected together to form an alkylene bridge of 4 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring;

25 R₁ and R₃, when v=1, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the carbon atoms to which they are attached a cyclohexane ring;

R₄ is lower alkyl, substituted lower alkyl, cycloalkyl-

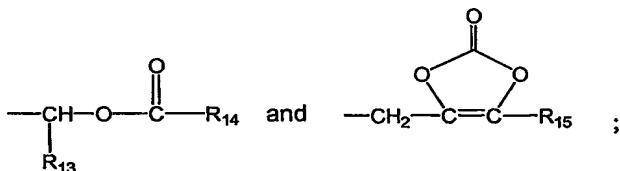
30 (CH₂)_w, aryl-(CH₂)_w, substituted aryl -(CH₂)_w or heteroaryl-(CH₂)_w;

R and R₄ may be connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring;

5 R and R₄ may be connected together to form an alkylene bridge of 4 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

R₅ is hydrogen, lower alkyl, substituted lower alkyl, cycloalkyl-(CH₂)_x-, aryl-(CH₂)_x-, substituted aryl-(CH₂)_x-, or heteroaryl-(CH₂)_x;

10 R₆ is hydrogen, R₇-CO-, or R₁₂-S-;
 R₇ is alkyl, substituted alkyl, cycloalkyl-(CH₂)_y, aryl-(CH₂)_y, substituted aryl-(CH₂)_y or heteroaryl-(CH₂)_y;
 R₈ and R₉ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl-(CH₂)_y, substituted aryl-(CH₂)_y, heteroaryl-(CH₂)_y,
 15



R₁₀ is alkyl, substituted alkyl, cycloalkyl-(CH₂)_y, aryl-(CH₂)_y, substituted aryl-(CH₂)_y or heteroaryl-(CH₂)_y;

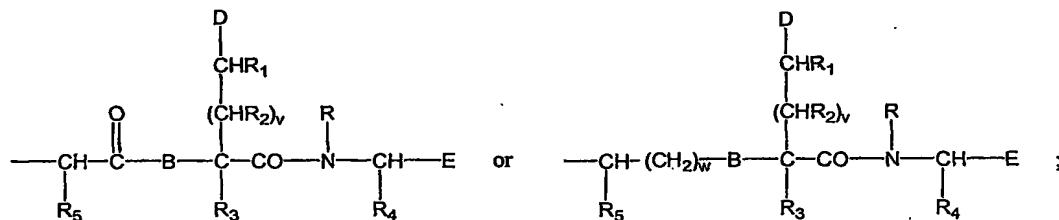
20 R₁₁ is hydrogen or lower alkyl; wherein the carbon bearing R₁ and the nitrogen bearing R₁₁, when v=1, may be directly connected together to form an azetidine ring;

R₁ and R₁₁, when v=0, may be connected together to form an alkylene bridge of 3 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

R_1 and R_{11} , when $v=1$, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a piperidine ring;

5 R_2 and R_{11} , when $v=1$, may be connected together to form an alkylene bridge of 2 carbon atoms representing with the nitrogen and carbon atoms to which they are attached a pyrrolidine ring; the alkylene bridge may be substituted by a lower alkyl or alkenyl group at either carbon;

10 R_{12} is alkyl, substituted alkyl, cycloalkyl- $(CH_2)_y$ -, aryl- $(CH_2)_y$ -, substituted aryl- $(CH_2)_y$ -, heteroaryl- $(CH_2)_y$ -,



in which case $-S-R_{12}$ completes a symmetrical disulfide;

R_{13} is hydrogen, lower alkyl, cycloalkyl or phenyl;

R_{14} is hydrogen, lower alkyl, lower alkoxy or phenyl;

15 R_{15} is lower alkyl or aryl- $(CH_2)_y$;

D is $-COOH$, $-SO_2H$, $-SO_3H$, $-PO_3H_2$, $-OSO_3H$ or $-OPO_3H_2$;

20 E is hydrogen, R_{12} , $-COOH$, $-CONH_2$, $-CONH$ (lower alkyl), $-CON$ (lower alkyl) $_2$, $-CONH-(CH_2)_z$ -aryl, $-CON(-CH_2)_z$ -aryl $_2$, $-CO-$ amino acid, $-CH_2COOH$, CH_2OH , $-CH_2CH_2OH$, or $-COOR_{16}$;

R_{16} is as previously defined for R_8 and R_9 ;

C is carbon;

H is hydrogen;

O is oxygen;

25 N is nitrogen;

S is sulfur;
P is phosphorus;
v is zero or one;
w is zero or an integer ranging from 1 to 4;
5 x is an integer ranging from 1 to 4;
y is zero or an integer ranging from 1 to 6; and
z is zero, one, two or three.

2. The compound as defined in claim 1, which is:

N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-
10 acetylamino)- succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-3-
phenyl-propionyl amino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-
propionylamino)-succinamic acid;
15 N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-4-
methyl-pentanoylamino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-3-
methyl-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-hydroxy-2-
20 mercapto-propionylamino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(3-hydroxy-2-
mercaptop-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-
hexanoylamino)-succinamic acid;
25 N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-4-
phenyl-butyrylamino)-succinamic acid;
N-[1-Carboxy-2-(1H-indol-3-yl)-ethyl]-3-(2-mercaptop-2-
phenyl-acetylamino)-succinamic acid;
3-(3-Biphenyl-4-yl-2-mercaptop-propionylamino)-N-[1-
30 Carboxy-2-(1H-indol-3-yl)-ethyl]-succinamic acid;

3-(3-(4-Benzyl-phenyl)-2-mercaptopropionylamino)-
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[3-(4-fluoro-
phenyl)-2-mercaptopropionylamino]-succinamic acid;
5 N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[2-mercaptopro-
(4-methoxy-phenyl)-propionylamino]-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(3-cyclohexyl-2-
mercaptopropionylamino)-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-[3-(1*H*-indol-3-
10 yl)-2-mercaptopropionylamino]-succinamic acid;
N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercaptopro-
naphthalen-2-yl-propionylamino)-succinamic acid;
N-(1-Carboxy-2-naphthalen-2-yl-ethyl)-3-(2-mercaptopro-
phenyl propionylamino)-succinamic acid;
15 N-(1-Carboxy-2-hydroxy-ethyl)-3-(2-mercaptopro-3-phenyl-
propionyl amino)-succinamic acid;
N-[1-Carboxy-2-(4-hydroxy-phenyl)-ethyl]-3-(2-
mercaptopro-3-phenyl-propionylamino)-succinamic acid;
N-[1-Carboxy-2-phenyl-ethyl]-3-(2-mercaptopro-3-phenyl-
20 propionyl amino)-succinamic acid;
N-(2-Biphenyl-4-yl-1-Carboxy-ethyl)-3-(2-mercaptopro-3-
phenyl-propionyl amino)-succinamic acid;
N-(1-Benzyl-2-hydroxy-ethyl)-3-(2-mercaptopro-3-phenyl-
propionyl amino)-succinamic acid;
25 N-[1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercaptopro-3-
phenyl-propionylamino)-succinamic acid;
4-[1-Carboxy-2-(1*H*-indol-3-yl)-ethylcarbamoyl]-4-(2-
mercaptopro-3-phenyl-propionylamino)-ethyl]-butyric acid;
N-[2-(1*H*-indol-3-yl)-methylcarbamoyl-ethyl]-3-(2-
30 mercapto-acetyl amino)-succinamic acid;

N-[1-(1-Carboxy-2-hydroxy-ethylcarbamoyl)-2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercaptop-3-phenyl-propionylamino)-succinamic acid;
N-[2-(1*H*-indol-3-yl)-methoxycarbonyl-ethyl]-3-(2-mercaptop-acetyl amino)-succinamic acid;

5 *N*-[2-(1*H*-indol-3-yl)-ethyl]-3-(2-mercaptop-3-phenyl-propionylamino)-succinamic acid;
 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid;
 3-[2-(4'-Cyano-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;

10 4-Hydroxycarbamoyl-3-[2-(4-pyridin-2-yl-phenyl)-ethylcarbamoyl]-butyric acid;
 4-Hydroxycarbamoyl-3-(4-phenyl-butylicarbamoyl)-butyric acid;

15 4-Hydroxycarbamoyl-3-(2-phenoxy-ethylcarbamoyl)-butyric acid;
 3-[2-(4'-Hydroxy-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;
 3-(2,2-Diphenyl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyrinic acid;

20 butyric acid;
 3-[2-(4'-Dimethylamino-biphenyl-4-yl)-ethylcarbamoyl]-4-hydroxycarbamoyl-butyric acid;
 4-Hydroxycarbamoyl-3-(5-hydroxy-pentylcarbamoyl)-butyric acid;

25 3-[(Biphenyl-4-ylmethyl)-carbamoyl]-4-hydroxycarbamoyl-butyric acid;
 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-5-hydroxycarbamoyl-pentanoic acid;
 N-[1-carboxy-2-(1*H*-indol-3-yl)-ethyl]-3-(3-phenyl-1-

30 phosphono-propylamino)-succinic acid; or

3-(2-Naphthalen-2-yl-ethylcarbamoyl)-pentanedioic acid.

3. The compound of claim 2, which is 3-(2-Biphenyl-4-yl-ethylcarbamoyl)-4-hydroxycarbamoyl-butyric acid.

4. A pharmaceutical composition comprising a 5 therapeutically effective amount of a compound of any one of claims 1 to 3 and a physiologically acceptable carrier or excipient.

5. A method for inhibiting PHEX comprising contacting PHEX with an inhibitory amount of a compound as recited in any one of claims 1 to 3.

10 6. A method for stimulating bone mass formation in a mammal comprising inhibiting PHEX with an effective amount of a compound as recited in any one of claims 1 to 3.

15 7. A method for treating or preventing a disease or condition associated with a phosphate metabolism defect comprising administering an effective amount of a compound as recited in any one of claims 1 to 3 to a mammal in need thereof.

8. A method as recited in claim 7, wherein said disease or condition is selected from the group consisting of hyperphosphatemia, hyperparathyroidism and renal insufficiencies.

20 9. A method for identifying PHEX substrates comprising
contacting a candidate with PHEX in the presence and in
the absence of a compound as recited in any one of claims 1 to 3; and
assessing PHEX biological activity on the candidate in the
25 presence and in the absence of the compound,

wherein the candidate compound is selected as a PHEX substrate when PHEX biological activity is measurably higher in the absence versus in the presence of the compound.

10. A use of a compound as recited in any one of
5 claims 1 to 3 for inhibiting PHEX.

11. A use of a compound as recited in any one of
claims 1 to 3 for stimulating bone mass formation in a mammal.

12. A use of a compound as recited in any one of
claims 1 to 3 for treating or preventing a disease or condition associated
10 with a phosphate metabolism.

13. A use of a compound as recited in claim 12,
wherein said disease or condition is selected from the group consisting of
hyperphosphatemia, hyperparathyroidism and renal insufficiencies.

14. A use of a compound as recited in any one of
15 claims 1 to 3, for identifying PHEX substrates comprising
contacting a candidate with PHEX in the presence and in
the absence of the compound; and
assessing PHEX biological activity on the candidate in the
presence and in the absence of the compound,
20 wherein the candidate compound is selected as a PHEX substrate when PHEX biological activity is measurably higher in the absence versus in the presence of the compound.